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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
08 398,555	03 03 1995	LINDA G CIMA	MIT6210	7254

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EXAMINER

RUSSEL, JEFFREY E

ART UNIT	PAPER NUMBER
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1654

DATE MAILED: 01 31 2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action**

Application No.

08/398.555

Applicant(s)

CIMA ET AL

Examiner

Jeffrey E. Russel

Art Unit

1654

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

**PERIOD FOR REPLY** [check either a) or b)]

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
- ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on \_\_\_\_\_. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);
- (b) ☐ they raise the issue of new matter (see Note below).
- (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: See attachment

3. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.
4. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☐ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: See attachment
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☐ For purposes of Appeal, the proposed amendment(s) a) ☒ will not be entered or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: \_\_\_\_\_

Claim(s) objected to: \_\_\_\_\_

Claim(s) rejected: 14-17 and 32

Claim(s) withdrawn from consideration: \_\_\_\_\_

8. ☐ The proposed drawing correction filed on \_\_\_\_\_ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_.
10. ☐ Other: \_\_\_\_\_

1. The proposed amendments to claims 14 and 32 specifying particular attachment agents raise new issues requiring further consideration and search. Specific attachment agents have not previously been claimed in this application. The proposed amendments would require the examiner to search for prior art on the specific attachment agents and to determine whether this new art can be combined with the references already applied against the claims.

The proposed amendments raise new issues under 35 U.S.C. 112, second paragraph. Firstly, it is not clear if the proposed amendments require a new positive process step of attaching the tether to the substrate using the specific attachment agents, or if the proposed amendments instead recite a product-by-process definition of the attachment between the tether and the substrate. Secondly, the proposed amended claims would be indefinite because they require covalent attachment of the tether to the substrate, whereas avidin-biotin binding is not covalent. Thirdly, the proposed amended claims would be indefinite because their Markush language is incorrect. The conjunction "and" does not occur before the last member of the Markush group, leaving the relationship between maleimide, carbodiimide, and the other attachment agents unclear.

Proposed amended claims 14 and 32 at pages 2-3 of the response are not clean copies of the amended claims, i.e. they incorrectly include amendment markings.

2. The obviousness rejection based upon Herweck et al in view of Merrill is maintained. It should be noted that because the rejected claims do not contain the limitation found in the claims of U.S. Patent No. 5,906,828 requiring that the growth effector molecules be attached to the substrate in a concentration effective to enhance the rate of target cell growth over the rate of target cell growth with soluble effector molecules and growth effector molecules adsorbed to a

substrate (emphasis added - this portion of the patent claim limitation was omitted from Applicants' argument at page 8, third paragraph), the rejected claims in the instant application can not be allowed on the same basis as the patented claims.

Concerning the arguments set forth in page 9, last paragraph, of Applicants' response, the first sentence of this paragraph merely restates the obviousness issue and does not provide any arguments as to why the combination of the references is not obvious. As to the second and third sentences in this statement, it is to be expected that when references are combined under 35 U.S.C. 103, each of the individual references will not teach or suggest one or more aspects of the claimed invention. These two sentences accurately point out aspects of the claimed invention which are not taught or suggested by the individual references. However, the fact that individual references do not teach or suggest the claimed invention does not address the issue as to whether or not the claimed invention is suggested by the prior art when considered as a whole.

The combination of Merrill and Herweck et al on the basis of a motivation to prevent thrombogenesis is not deemed to be hindsight justification. As shown by Merrill at column 2, lines 17-23, thrombogenesis is a concern to one of ordinary skill in the art when blood contact with a biomedical device occurs.

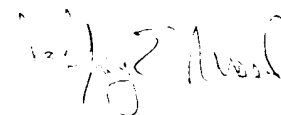
Herweck et al in combination with Merrill '264 is deemed to suggest enhanced cell growth without internalization. Herweck et al teach an enhanced rate of growth. Tethering of the bioactive materials of Herweck et al through the polyethylene oxide of Merrill '264 would still result in the bioactive materials being present at the implantation site, and therefore an enhanced rate of growth would have been expected to be maintained. Note that motivation to combine references under 35 U.S.C. 103 need not be the same as Applicants' motivation. See

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MPEP 2144. Accordingly, in order to establish prima facie obviousness, the examiner need not establish that it is obvious to combine Herweck et al and Merrill '264 for the express purpose of preventing internalization of growth effector molecules.

3. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (703) 308-3975. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Brenda Brumback can be reached at (703) 306-3220. The fax number for Art Unit 1654 for formal communications is (703) 305-3014; for informal communications such as proposed amendments, the fax number (703) 746-5175 can be used. The telephone number for the Technology Center 1 receptionist is (703) 308-0196.



Jeffrey E. Russel

Primary Patent Examiner

Art Unit 1654

JRussel

January 27, 2003